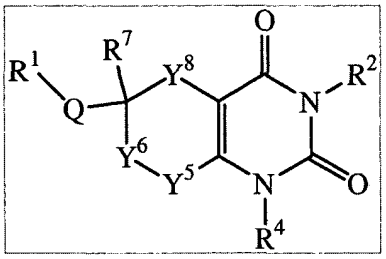
CLAIMS

What is claimed is:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is independently selected from:

C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl; and

Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-$S(O)_2$;

H_2N;

(C_1-C_6 alkyl)-N(H);

(C_1-C_6 alkyl)$_2$-N;

(C_1-C_6 alkyl)-C(O)O-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)$_m$;

$H_2NS(O)_2$-(C_1-C_8 alkylenyl);

(C_1-C_6 alkyl)-N(H)S(O)$_2$-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)$_2$-NS(O)$_2$-(C_1-C_8 alkylenyl)$_m$;

3- to 6-membered heterocycloalkyl-(G)$_m$;

Substituted 3- to 6-membered heterocycloalkyl-(G)$_m$;

5- or 6-membered heteroaryl-(G)$_m$;

Substituted 5- or 6-membered heteroaryl-(G)$_m$;

(C_1-C_6 alkyl)-S(O)$_2$-N(H)-C(O)-(C_1-C_8 alkylenyl)$_m$; and

(C_1-C_6 alkyl)-C(O)-N(H)-S(O)$_2$-(C_1-C_8 alkylenyl)$_m$;

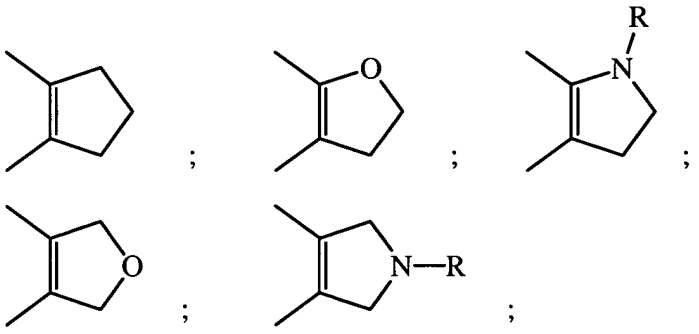
wherein each substituent on a carbon atom may further be independently selected from:

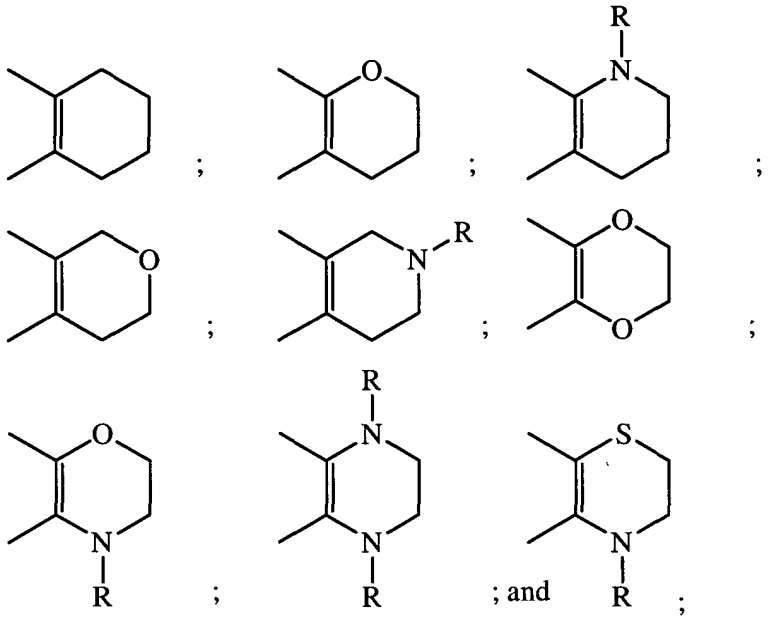
Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





R is H or C_1-C_6 alkyl;

G is CH_2; O, S, S(O); or $S(O)_2$;

m is an integer of 0 or 1;

R^7 is independently selected from the groups:

H;

CH_3;

CH_3O;

$CH=CH_2$;

HO;

CF_3;

CN;

HC(O);

$CH_3C(O)$;

HC(NOH);

H_2N;

(CH_3)-N(H);

$(CH_3)_2$-N;

$H_2NC(O)$;

(CH_3)-N(H)C(O);

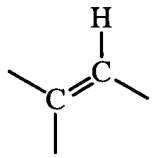
$(CH_3)_2$-NC(O);

halo; and

CO_2H;

Y^5 and Y^8 are each independently CH_2, C(O), O, S, S(O), $S(O)_2$, or $N(R^5)$; or

R^7 and Y^8 may be taken together with the carbon atom to which they are both attached to form a group selected from: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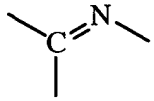
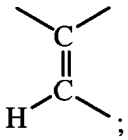

;

Y^6 is CH_2 or C(O); or

Y^6 and R^7 may be taken together with the carbon atom to which they are both attached to form a group:


;

wherein R^7 is not simultaneously taken together with Y^6 and Y^8;

R^4 and R^5 are each independently selected from the groups:

H;

CH_3;

CH_3O;

$CH=CH_2$;

HO;

CF_3;

CN;

HC(O);

$CH_3C(O)$;

HC(NOH);

H_2N;

(CH_3)-N(H);

$(CH_3)_2$-N;

$H_2NC(O)$;

(CH_3)-N(H)C(O); and

$(CH_3)_2$-NC(O);

Q is selected from:

OC(O);

$CH(R^6)C(O)$;

$OC(NR^6)$;

$CH(R^6)C(NR^6)$;

$N(R^6)C(O)$;

$N(R^6)C(S)$;

$N(R^6)C(NR^6)$;

$N(R^6)CH_2$;

SC(O);

$CH(R^6)C(S)$;

$SC(NR^6)$;

trans-(H)C=C(H);

cis-(H)C=C(H);

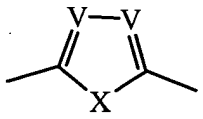
C≡C;

$CH_2C{\equiv}C$;

$C{\equiv}CCH_2$;

$CF_2C{\equiv}C$; and

$C{\equiv}CCF_2$;



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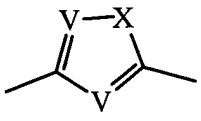

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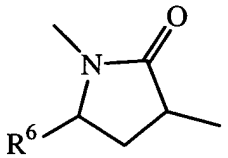

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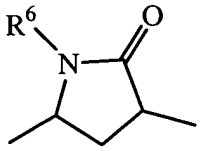

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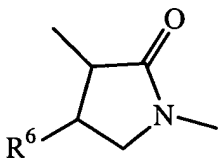

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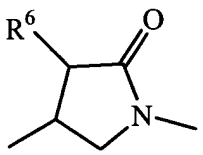
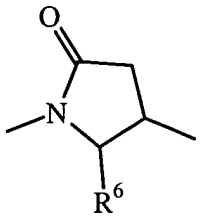


; and



;

Each R^6 independently is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C_1-C_6 alkyl);

Each V is independently C(H) or N;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any $(C_1\text{-}C_6$ alkyl$)_2$-N group, the $C_1\text{-}C_6$ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y^6 is C(=O).

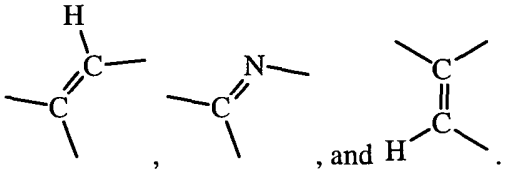
3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y^6 is CH_2.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^6)C(O)$.

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to Claim 1, wherein R^7 is H.

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein R^7 and Y^8 are taken together with the carbon atom to which they are both attached to form a group selected from:



, , and .

8. The compound according to any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^1 is independently selected from:

Phenyl-($C_1\text{-}C_8$ alkylenyl);

Substituted phenyl-($C_1\text{-}C_8$ alkylenyl);

5- or 6-membered heteroaryl-($C_1\text{-}C_8$ alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

R^2 is independently selected from:

Phenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

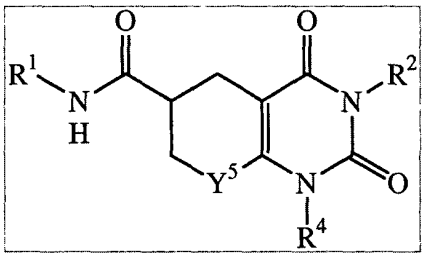
8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$; and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$;

wherein m is an integer of 0 or 1; and

wherein each group and each substituent is independently selected.

9. A compound of Formula II



II

or a pharmaceutically acceptable salt thereof.

10. The compound of Formula II according to Claim 9, selected from:

3-(3,5-Difluoro-4-hydroxy-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid 3-methoxy-benzylamide;

3-(3,4-Difluoro-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

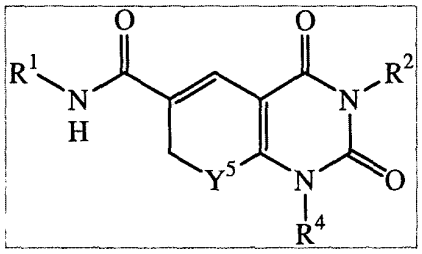
3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide; and

3-(3,4-Difluoro-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

or a pharmaceutically acceptable salt thereof.

11. A compound of Formula III



III

or a pharmaceutically acceptable salt thereof.

12. The compound of Formula III according to Claim 11, selected from:

3-(3,5-Difluoro-4-hydroxy-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 3-methoxy-benzylamide;

3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-[4-(3-Ethyl-ureido)-benzyl]-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,5,6,7,8-octahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide; and

3-(4-Cyano-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

14. The pharmaceutical composition according to Claim 13, comprising a compound according to Claim 10 or 12, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

15. A method for treating arthritis, comprising administering to a patient suffering from an arthritis disease a nontoxic antiarthritic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

16. The method according to Claim 15, wherein the arthritis is osteoarthritis or rheumatoid arthritis.

17. The method according to Claim 16, wherein the compound according to Claim 1 is a compound according to Claim 10 or 12.